

Claims

1. A process for the manufacture of (*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-enoic acid calcium salt, which process comprises mixing of a solution of calcium chloride with a solution of a water-soluble salt of (*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-enoic acid, wherein the process parameters are selected to give a product which demonstrates improved efficiency of filtration.
2. A process according to claim 1 comprising mixing of a solution of calcium chloride with a solution of a water-soluble salt of (*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-enoic acid such that the addition temperature is selected to give a product which demonstrates improved efficiency of filtration.
3. A process according to any preceding claim wherein the addition temperature is 30-45°C.
4. A process according to any preceding claim comprising mixing of a solution of calcium chloride with a solution of a water-soluble salt of (*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-enoic acid such that the addition time is selected to give a product which demonstrates improved efficiency of filtration.
5. A process according to any preceding claim wherein the addition time is 5 to 60 minutes.
6. A process according to any preceding claim comprising mixing of a solution of calcium chloride with a solution of a water-soluble salt of (*E*)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3*R*,5*S*)-3,5-dihydroxyhept-6-enoic acid such that the hold time is selected to give a product which demonstrates improved efficiency of filtration.

7. A process according to any preceding claim wherein the hold time is at least 10 minutes.
8. A process according to any claim which comprises addition of a solution of calcium chloride to a solution of a water-soluble salt of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid over 5 to 60 minutes at a temperature of 30 to 45°C, holding the mixture at a temperature of 30 to 45°C for at least 10 minutes, filtering, optionally washing, and drying of the resultant product.
9. A process according to any preceding claim wherein the addition temperature is adjusted to give a product with a specific surface area less than or equal to 1 m²/g (measured by Fisher technique).
10. A process according to any preceding claim wherein the addition temperature, addition time and hold time are adjusted to give a product with a specific surface area less than or equal to 1 m²/g (measured by Fisher technique).
11. A process according to any preceding claim wherein the addition temperature, addition time and hold time are adjusted to give a product with a specific surface area less than or equal to 0.5 m²/g (measured by Fisher technique).
12. A process according to any preceding claim wherein the product has a paste strength of more than about 45%w/w.
13. A process according to any preceding claim in which the product paste strength after a maximum of 15 minutes filtration on a laboratory scale is at least 50% w/w.
14. A process according to any one of claims 1 to 11 wherein the product is obtained with a paste strength of more than about 70%w/w.
15. A process according to any preceding claim wherein the water soluble salt of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid is an alkali metal salt.

16. A process according to any preceding claim wherein the water soluble salt of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid is the sodium salt.
- 5 17. A process according to any one of claims 1 to 14 wherein the water soluble salt of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid is an ammonium salt, a methylamine salt or a TRIS salt.
- 10 18. A process according to any one of claims 1 to 14 wherein the water soluble salt of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid is generated from the ammonium salt.
- 15 19. A process according to any one of claims 1 to 14 wherein the solution of the water soluble salt is generated from (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid or a salt thereof.
- 20 20. A process according to claim 19 wherein the water soluble salt is the sodium salt.
21. A process according to claim 20 wherein the sodium salt is generated by treatment of an amine salt of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid with a sodium base.
- 25 22. A process according to claim 21 where sodium base is sodium hydroxide.
23. A product obtainable by a process as claimed in any preceding claim.
- 30 24. A product obtained by a process as claimed in any preceding claim.